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Genome FAQs

Relatively Speaking

The many visitors (some 7000 a month) to the Human Genome Project Information Web site ask us interesting questions about genetics and the Human Genome Project. Some we answer directly, and others we refer to leading researchers in relevant fields. From time to time, HGN will print answers to selected frequently asked questions (FAQs). These and other FAQs will also be posted to the Web site (*http://www.ornl.gov/hgmis/*).

The following reply, supplied by researcher Lisa Stubbs [Oak Ridge National Laboratory (ORNL)], was prompted by a recent query sent by a New Zealand ethicist. Stubbs conducts research on mouse-human comparative genome mapping for the DOE Human Genome Program.

FAQ:How closely related are mice and humans? What percentage of genes are the same?

Mice and humans (indeed, most or all mammals including dogs, cats, rabbits, monkeys, and apes) have roughly the same number of nucleotides in their genomes about 3 billion base pairs. This comparable DNA content implies that all mammals contain more or less the same number of genes, and indeed our work at ORNL and the work of many others have provided evidence to confirm that notion.

I know of only a few cases in which no mouse counterpart can be found to correspond to a particular human gene, but otherwise we see essentially a one-to-one correspondence between genes in the two species. The exceptions generally appear to be of a particular type genes that arise when an existing sequence is duplicated and changed enough to perform a new function. These make up a small percentage of the total genes, in my opinion. We won't know for certain until both genomes are sequenced, but I believe the number won't be significantly larger than 1 to 5%.

The differences between mice and humans are not in the number of genes we each carry but in the structure of genes and the activities of their protein products. Gene for gene, we are very similar to mice. What really matters is that around 100,000 very subtle changes add together to make quite different organisms. Further, genes and proteins interact in complex ways that multiply the functions of each. In addition, a gene can produce more than one protein product through alternative splicing or post-translational modification. A gene can produce more or less protein in different cells at various times in response to developmental or environmental cues, and many proteins can express disparate functions in various biological contexts. Thus, subtle distinctions are multiplied by the more than 100,000 estimated genes.

The often-quoted statement that we share over 90% of our genes with apes actually should be put another way. That is, we share virtually all our genes with apes. However, on average, a single related set of ape and human genes would differ in DNA sequence by about 10%. For mouse, it is more like 20 to 30%, with a lot of variation from gene to gene in those differences (e.g., some mouse and human gene products are almost identical). Some of those 10 to 30% nucleotide changes would be "neutral" and would not result in production of a significantly altered protein. Others, but probably only a relatively small percentage, would introduce changes that could substantially alter what the protein does.

Put these alterations in the context of known human inherited diseases: If a certain nucleotide is changed in a particular gene, for example, a person can develop sickle cell disease, cystic fibrosis, or breast cancer. A single nucleotide difference can alter protein function in such a way that it causes a terrible tissue malfunction. However, many other single-nucleotide changes in the same gene would do nothing harmful at all. Evolutionary changes are the same way some are neutral, some subtle, and some dramatic. Add them all together, and they can make quite an impact and account for the huge differences we see among organisms.

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